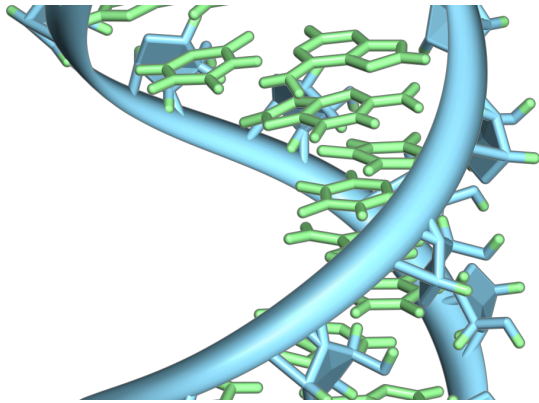


New process yields more, purer RNA at a fraction of the cost

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A hairpin loop from a pre-mRNA. Highlighted are the nucleobases (green) and the ribose-phosphate backbone (blue). Note that this is a single strand of RNA that folds back upon itself. Credit: Vossman/ Wikipedia

Researchers at the University of Massachusetts Amherst recently unveiled their discovery of a new process for making RNA. The resulting RNA is purer, more copious and likely to be more cost-effective than any previous process could manage. This new technique removes the largest stumbling block on the path to next-generation RNA therapeutic drugs.

If DNA is the blueprint that tells the cells in our bodies what proteins to make and for what purposes, RNA is the messenger that carries DNA's instruction to the actual [protein](#)-making machinery within each cell. Most of the time this process works flawlessly, but when it doesn't, when the body can't make a protein it needs, as in the case of a disease like cystic fibrosis, serious illness can result.

One method for treating such protein deficiencies is with therapeutics that replace the missing proteins. But researchers have long known that it's more effective when the body can make the

protein it needs itself. This is the goal of an emerging field of medicine—RNA therapeutics. The problem is, the current methods of producing lab-made RNA can't deliver RNA that is pure enough, in enough quantities in a way that's cost-effective. "We need lots of RNA," says Elvan Cavaç, lead author of the paper that was recently published in the *Journal of Biological Chemistry*, MBA student at UMass Amherst, and a recent Ph.D. graduate in chemistry, also from UMass. "We've developed a novel process for producing pure RNA, and since the process can reuse its ingredients, yielding anywhere between three and ten times more RNA than the conventional methods, it also saves time and cost."

The problem with impure RNA is that it can trigger reactions, like swelling, that can be harmful, and even life-threatening. For example, impure RNA can cause inflammation in the lungs of a patient with [cystic fibrosis](#). Conventionally manufactured RNA has to undergo a lengthy and expensive process of purification. "Rather than having to purify RNA," says Craig Martin, the paper's senior author and professor of chemistry at UMass, "we've figured out how to make clean RNA right from the start."

The process that Cavaç, Martin and their co-authors detail involves first increasing the salinity of the solution in which the RNA is generated, which inhibits the runaway production of RNA that leads to impurity. In this process, an enzyme called T7 RNA polymerase is "tethered" to a microscopic magnetic bead alongside a DNA promoter template—a specific sequence of DNA that codes for a specific RNA. Once the polymerase and DNA promoter interact, they produce RNA whose purity is ensured by the surrounding saline solution. "Our method," says Martin, "can be more than ten times better at producing pure RNA than current processes."

Cavaç, Martin and their colleagues are now turning

to experiments that will allow them to scale up the production of RNA to satisfy society's needs. "The real goal here," says Martin, "is to have a 'flow reactor,' or a continuous pipeline into which you can slowly feed the ingredients and have pure RNA continuously come out the other end."

More information: Elvan Cavac et al, High salt transcription of DNA co-tethered with T7 RNA polymerase to beads generates increased yields of highly pure RNA, *Journal of Biological Chemistry* (2021). DOI: [10.1016/j.jbc.2021.100999](https://doi.org/10.1016/j.jbc.2021.100999)

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